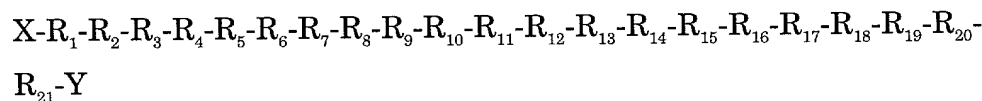## CLAIMS

What is claimed is:

5   **1.** A peptide fragment of a viral Macrophage Inflammatory Protein-II (vMIP-II) (SEQ. ID. NO: 1), wherein said fragment selectively prevents CXCR4 signal transduction and coreceptor function in mediating an entry of an HIV-1.

10   **2.** The peptide fragment of **Claim 1**, wherein said fragment comprises an amino-terminal end of said vMIP-II.

3. The peptide fragment of **Claim 2**, wherein said amino-terminal end comprises amino acid residues 1-21 (V1, SEQ ID NO: 2), or any

15   subfragments therein.

4. The peptide fragment of **Claim 1**, wherein said fragment is a lead compound for development of novel small molecular agents to prevent HIV-1 from entering a cell.
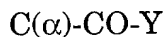
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5. A peptide of the formula

X-R_1-R_2-R_3-R_4-R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-Y

wherein:

25   X is a substituent attached on the N-terminal of a peptide, X can be H, CH_3CO, C_6H_5CO, or $C_6H_5CH_2CO$;

Y is a substituent attached on the C-terminal of a peptide with the following general structure,

$$C(\alpha)\text{-}CO\text{-}Y$$

30   Y can be OH, NH_2, OCH_3, $OCH_2C_6H_5$, or $NHCH_3$; Y can be from zero to nine amino acids,

R_1 is Ile, Leu, Val, or Phe;

28

R_2 is Gly, Ala;

R_3 is Ala, Gly;

R_4 is Ser, Thr, or Tyr;

R_5 is Trp, Phe, Tyr;

5   R_6 is His, Lys, Arg, or Tyr;

R_7 is Arg, His, or Lys;

R_8 is Pro, Leu, or Val;

R_9 is Asp, Glu, Arg, or Lys;

R_{10} is Lys, Arg, or His;

10   R_{11} is Cys, Ser, or Ala;

R_{12} is Cys, Ser, or Ala;

R_{13} is Ile, Leu, or Val;

R_{14} is Gly, Ala;

R_{15} is Tyr, Thr, Ser;

15   R_{16} is Gln, Asn, Arg, or Lys;

R_{17} is Lys, Arg, or His;

R_{18} is Arg, His, or Lys;

R_{19} is Pro, Leu, or Val;

R_{20} is Ile, Leu, or Val;

20   R_{21} is Pro, Leu, or Val;

and if R_{11} is Cys then R_{12} can be Cys, penicillamine or tertiary

butyloxycarbonyl-a-aminobutyric acid;

if R_{12} is Cys then R_{11} can be Cys, penicillamine, tertiary

butyloxycarbonyl-a-aminobutyric acid, and,

25   R_{11} and R_{12} can be penicillamine, or tertiary butyloxycarbonyl-a-

aminobutyric acid;

and, R_{11} and R_{12} can be Ala.

6. The peptide of **Claim** 5, wherein a preferred embodiment,

30   comprises

X can be H, or CH_3CO; Y can be OH,or NH_2; and,R_1 is Leu, R_2 is

Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is

Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

7. The peptide of **Claim 5**, wherein a most preferred embodiment, comprises X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

8. The peptide of **Claim 5**, wherein a preferred embodiment comprises a C-terminal truncation peptide contaiings at least the following fragment:

$X-R_1-R_2-R_3-R_4-R_5-R_6-R_7-R_8-Y$, and wherein;

R_1 is Ile, Leu, or Phe;

R_2 is Gly, Ala, or Val;

R_3 is Ala, Val, or Gly;

R_4 is Ser, Thr, or Tyr;

R_5 is Trp, Phe, Tyr, or Leu;

R_6 is His, Lys, Arg, or Trp;

R_7 is Arg, His, or Lys;

R_8 is Pro, Leu, or Val.

and, a C-terminal truncation peptide preferably containing at least a following fragment, wherein X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys.

9. The peptide of **Claim 1**, wherein said peptide comprises between 3-30 amino acids, preferably 8-21 amino acids.

10. A synthetic peptide, wherein each amino acid of said synthetic peptide is a D amino acid, having the formula:

$X-R_{1d}-R_{2d}-R_{3d}-R_{4d}-R_{5d}-R_{6d}-R_{7d}-R_{8d}-R_{9d}-R_{10d}-R_{11d}-R_{12d}-R_{13d}-R_{14d}-R_{15d}-R_{16d}-R_{17d}-R_{18d}-R_{19d}-R_{20d}-R_{21d}-Y$, wherein,

X is a substituent attached on the N-terminal of a peptide, X can be
H, CH_3CO, C_6H_5CO, or $C_6H_5CH_2CO$; and

Y is a substituent attached on the C-terminal of a peptide with the
following general structure:

$C(\alpha)$-CO-Y, wherein Y can be OH, NH_2, OCH_3, $OCH_2C_6H_5$, or $NHCH_3$
and Y can be from zero to nine amino acids.

R_{1d} is Ile, Leu, Val, or Phe;

R_{2d} is Gly, Ala;

R_{3d} is Ala, Gly;

R_{4d} is Ser, Thr, or Tyr;

R_{5d} is Trp, Phe, or Tyr;

R_{6d} is His, Lys, Arg, or Tyr;

R_{7d} is Arg, His, or Lys;

R_{8d} is Pro, Leu, or Val;

R_{9d} is Asp, Glu, Arg, or Lys;

R_{10d} is Lys, Arg, or His;

R_{11d} is Ala, Cys, or Ser;

R_{12d} is Ala, Cys, or Ser;

R_{13d} is Ile, Leu, or Phe;

R_{14d} is Gly, Ala;

R_{15d} is Tyr, Thr, Ser;

R_{16d} is Gln, Asn, Arg, or Lys;

R_{17d} is Lys, Arg, or His;

R_{18d} is Arg, His, or Lys;

R_{19d} is Pro, Leu, or Val;

R_{20d} is Ile, Leu, or Val;

R_{21d} is Pro, Leu, or Val;

and wherein:

if R_{11d} is Cys then R_{12d} can be Cys, penicillamine or tertiary
butyloxycarbonyl-a-aminobutyric acid;

if R_{12d} is Cys then R_{11d} can be Cys, penicillamine, or tertiary
butyloxycarbonyl-a-aminobutyric acid;

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and,

R_{11d} and R_{12d} can be penicillamine, or tertiary butyloxycarbonyl-a-aminobutyric acid;

and, R_{11d} and R_{12d} can be Ala.

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11. The peptide of **Claim 10**, wherein a preferred embodiment comprises the following formula:

X can be H, CH_3CO; Y can be OH, or NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is

10   Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is Pro.

12. The peptide of **Claim 10**, wherein a most preferred

15   embodiment comprises the following formula:

X is H, Y is NH_2; and,R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is Pro.

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13. The peptide of **Claim 10**, wherein a preferred C-terminal truncation peptide comprising at least the following fragment:

X-R_{1d}-R_{2d}-R_{3d}-R_{4d}-R_{5d}-R_{6d}-R_{7d}-R_{8d}-Y

and wherein;

25   R_{1d} is Ile, Leu, or Phe;

R_{2d} is Gly, Ala, or Val;

R_{3d} is Ala, Val, or Gly;

R_{4d} is Ser, Thr, or Tyr;

R_{5d} is Trp, Phe, Tyr, or Leu;

30   R_{6d} is His, Lys, Arg, or Trp;

R_{7d} is Arg, His, or Lys;

R_{8d} is Pro, Leu, or Val.

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14. The peptide of **Claim 10**, wherein a more preferably C-terminal truncation peptide comprises at least the following fragment;

X is H, Y is NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d}
5 is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys.

15. The peptide of **Claim 10**, comprising between 3-30 amino acids, preferably 8-21 amino acids.

10 **16**. The peptide of **Claim 5**, wherein said peptide comprises a reversed form of said formula, comprising,

X-R_{21}-R_{20}-R_{19}-R_{18}-R_{17}-R_{16}-R_{15}-R_{14}-R_{13}-R_{12}-R_{11}-R_{10}-R_9-R_8-R_7-R_6-R_5-R_4-R_3-R_2-R_1-Y

wherein an amino acid is in an L form or as naturally occurring
15 amino acid.

17. The peptide of **Claim 16**, wherein a preferred embodiment, comprises

X can be H, or CH_3CO; Y can be OH,or NH_2; and,R_1 is Leu, R_2 is
20 Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

18. The peptide of **Claim 16**, wherein a most preferred
25 embodiment, comprises X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

30 **19**. The peptide of **Claim 16**, wherein a preferred embodiment comprises a C-terminal truncation peptide contaiings at least the following fragment:

33

$X-R_1-R_2-R_3-R_4-R_5-R_6-R_7-R_8-Y$, and wherein;

R_1 is Ile, Leu, or Phe;

R_2 is Gly, Ala, or Val;

R_3 is Ala, Val, or Gly;

5   R_4 is Ser, Thr, or Tyr;

R_5 is Trp, Phe, Tyr, or Leu;

R_6 is His, Lys, Arg, or Trp;

R_7 is Arg, His, or Lys;

R_8 is Pro, Leu, or Val.

10   and, a C-terminal truncation peptide preferably containing at least a following fragment, wherein X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys.

15   **20**. The peptide of **Claim 16**, wherein said peptide comprises between 3-30 amino acids, preferably 8-21 amino acids.

21. The peptide of **Claim 5**, wherein said peptide comprises a reversed form of said formula, comprising

20     $X-R_{21d}-R_{20d}-R_{19d}-R_{18d}-R_{17d}-R_{16d}-R_{15d}-R_{14d}-R_{13d}-R_{12d}-R_{11d}-R_{10d}-R_{9d}-R_{8d}-R_{7d}-R_{6d}-R_{5d}-R_{4d}-R_{3d}-R_{2d}-R_{2d}-Y$, wherein an amino acid is in a D form or as an unnaturally occurring amino acid.

22. The peptide of **Claim 21**, wherein a preferred embodiment

25   comprises the following formula:

X can be H, CH_3CO; Y can be OH, or NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is

30   Pro.

23. The peptide of **Claim 21**, wherein a most preferred embodiment comprises the following formula:

X is H, Y is NH$_2$; and, R$_{1d}$ is Leu, R$_{2d}$ is Gly, R$_{3d}$ is Ala, R$_{4d}$ is Ser, R$_{5d}$ is Trp, R$_{6d}$ is His, R$_{7d}$ is Arg, R$_{8d}$ is Pro, R$_{9d}$ is Asp, R$_{10d}$ is Lys, R$_{11d}$ is Ala, R$_{12d}$ is Cys, R$_{13d}$ is Leu, R$_{14d}$ is Gly, R$_{15d}$ is Tyr, R$_{16d}$ is Gln, R$_{17d}$ is Lys, R$_{18d}$ is Arg, R$_{19d}$ is Pro, R$_{20d}$ is Leu, R$_{21d}$ is Pro.

23. The peptide of **Claim 21**, wherein a preferred C-terminal truncation peptide comprising at least the following fragment:

X-R$_{1d}$-R$_{2d}$-R$_{3d}$-R$_{4d}$-R$_{5d}$-R$_{6d}$-R$_{7d}$-R$_{8d}$-Y

and wherein;

R$_{1d}$ is Ile, Leu, or Phe;

R$_{2d}$ is Gly, Ala, or Val;

R$_{3d}$ is Ala, Val, or Gly;

R$_{4d}$ is Ser, Thr, or Tyr;

R$_{5d}$ is Trp, Phe, Tyr, or Leu;

R$_{6d}$ is His, Lys, Arg, or Trp;

R$_{7d}$ is Arg, His, or Lys;

R$_{8d}$ is Pro, Leu, or Val.

24. The peptide of **Claim 21**, wherein a more preferably C-terminal truncation peptide comprises at least the following fragment;

X is H, Y is NH$_2$; and, R$_{1d}$ is Leu, R$_{2d}$ is Gly, R$_{3d}$ is Ala, R$_{4d}$ is Ser, R$_{5d}$ is Trp, R$_{6d}$ is His, R$_{7d}$ is Arg, R$_{8d}$ is Pro, R$_{9d}$ is Asp, R$_{10d}$ is Lys.

25. The peptide of **Claim 21**, comprising between 3-30 amino acids, preferably 8-21 amino acids.

26. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 5**.

27. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 10**.

28. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 16**.

29. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 21**.

30. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 5**.

31. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 10**.

32. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 16**.

33. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 21**.

34. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 5.**

35. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 10**.

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36. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 16**.

36. A method of treating infection by HIV-1, comprising

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administering to an individual an effective amount of a peptide according to **Claim 21**.

37. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4,

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comprising contacting said cells with a peptide according to **Claim 5**

38. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4,

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comprising contacting said cells with a peptide according to **Claim 10.**

39. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4,

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comprising contacting said cells with a peptide according to **Claim 16.**

40. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4,

30

comprising contacting said cells with a peptide according to **Claim 21.**

41. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 5**.

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42. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 10**.

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43. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 46**.

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44. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 21**.

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